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Selective targeted cerebral revascularization via microscope integrated Indocyanine green videoangiography technology.

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Abbreviations

CT: Computed Tomography; CT-A: Computed Tomography Angiography; DSA: Digital Subtraction Angiography; EC-IC: Extra-to-intracranial; ICG: Indocyanine Green; ICG-VA: Indocyanine Green Video Angiography; MCA: Middle Cerebral Artery; STA: superficial temporal artery; STA-MCA: superficial temporal artery to middle cerebral artery

SUMMARY

Protective or flow replacement bypass surgery has an important role in the management of complex middle cerebral artery (MCA) aneurysms. Protective bypass is useful when prolonged temporary arterial occlusion is

needed for clip reconstruction. Flow replacement bypass is instead important when aneurysmal trapping is the treatment of choice, to supply permanent collateral blood flow to the brain distal to the "trapped" vessel. In both cases the identification of the correct recipient artery is an essential surgical step. When a superficial (cortical) artery is chosen as recipient, it has to represent indeed a distal branch of the involved (temporary or permanently occluded) vessel.

Herein we illustrate a technique for selective-targeted revascularization based on the use of Indocyanine green video angiography (ICG-VA), a microscope-integrated intraoperative tool nowadays known to provide real-time assessment of the cerebral circulation with distinct visualization of arterial, capillary and venous angiographic phases. The technique is founded on the analysis of differences in the timing of filling of M4 vessels seen on serial ICG-Vas. It enables reliable identification of the cortical recipient and eliminates the risk of erroneous revascularization of non-involved territories. The surgical decision making of two patients treated for complex MCA aneurysms with selective-targeted bypass is presented.

Key words: cerebral revascularization; complex aneurysms; Indocyanine Green Video Angiography, ICG-VA; MCA aneurysms; bypass recipient artery; selective EC-IC bypass; STA-MCA bypass.

INTRODUCTION

Complex MCA aneurysms not amenable to selective clipping or coiling are frequently treated by clip reconstruction or by aneurysm trapping. In these cases, respectively a protective or a flow replacement bypass is of importance in order to avoid ischemic consequences. In fact, a protective bypass is useful when a prolonged arterial occlusion (parent artery or aneurysmal branch) is necessary for a safe clip reconstruction, while a flow replacement bypass permits to supply collateral blood flow to the brain distal to a permanently occluded (trapped) vessel [7, 9-10, 13-14].

When microsurgical dissection of the peri-aneurysmal angioanatomy can be safely performed, the selection of a recipient artery among the vessels exposed within the dissected Sylvian fissure is a valid option, for instances a M2 or M3 segment of the MCA [10]. When dissection of the Sylvian fissure is considered more difficult or risky or when avoiding a deep site for the anastomosis is preferred, a superficial cortical recipient artery (namely a M4 segment of MCA) can be chosen as recipient instead [14]. Because the goal of the bypass is the preservation of blood flow in the territory fed by the vessel that needs to be occluded (temporary or permanently) for final

aneurysm treatment, it is very important that the recipient artery represents a distal branch of the trapped vessel indeed.

Despite the use of angioanatomical landmarks, neuroimaging, neuronavigation and stereotactic modalities [2, 4, 8] to identify the correct recipient, the risk of revascularization into a wrong territory still exists. Revascularization of the wrong territory obviously would lead to possible severe ischemic effects [2, 14].

In this manuscript we describe a technique for selective identification of a cortical (M4) recipient artery during extra-to-intracranial (EC-IC) bypass surgery. The technique is based on the use of microscope-integrated near-infrared ICG-VA that is known as a reliable and non-invasive technique introduced in neurosurgery for intraoperative observation and documentation of blood flow of large and small vessels [3, 11]. We recently reported this technique describing our experience in the treatment of 7 patients with complex MCA aneurysms: three illustrative case were presented. Here we further describe the possible application of the technique and illustrate the cases of two different patients.

MATERIAL AND METHODS

Patients

The surgical decision-making of two patients treated for complex MCA aneurysms with selective-targeted EC-IC bypass is reported. The patients underwent pre-operative neuroimaging consisting of computed tomography (CT) scan, CT-angiography (CT-A) and digital subtraction angiography (DSA) with 3D reconstructions in order to optimally define the peri-aneurysmal angioanatomy. Control angiography (CT-A or DSA) was performed in the first 72h after surgery. In one patient (illustrative case 2) a radiological angiographic follow-up was done at 3 months as well. Functional health of the two patients was assessed preoperatively and at 3-month follow-up.

Intraoperative microscope integrated ICG-VA

A standard Indocyanine green (ICG) dose of 25 mg dissolved in 5 mL of water was injected into a central vein as a bolus, so the field of interest was illuminated with near-infrared light emitted by a commercially available surgical microscope (OPMI® Pentero™, The Carl Zeiss Co, Oberkochen, Germany). The ICG-VA video was recorded for further analysis. ICG-VA is repeated as many times as needed within the daily dose limit of ICG (5 mg/kg), waiting at least 10 minutes between two consecutive intravenous ICG injections.

Identification of the recipient artery

Real-time ICG-VA is used for the visualization and the analysis of the cortical vasculature at the craniotomy site as well as for the distinct evaluation of arterial, capillary and venous phases of cortical peri-Sylvian fissure vessels, with excellent image quality, spatial and temporal resolution [3, 11]. The presented technique for selective targeted bypass is based on the analysis of the difference in timing of the fluorescence of M4 cortical vessels seen on serial ICG-VAs.

A delayed (asymmetric) fluorescence of cortical M4 vessels may be visualized either primarily (on a *baseline ICG-VA*) or secondarily (on a *provoked ICG-VA*, after temporary occlusion of the aneurysm parent artery or an aneurysmal branch). These situations are called primary and secondary identification respectively (see table 1).

Primary identification	A delayed (asymmetric) fluorescence can be *primarily* seen on the *baseline ICG-VA*. In this case no temporary occlusion of arteries is performed. Such a delay can be caused either by stenosis/occlusion of an aneurysmal branch or increased resistance to flow (i.e.: turbulent flow in the aneurysm, the presence of serpiginous aneurysm).
Secondary identification	A delayed (asymmetric) fluorescence can be *secondarily* detected after *provocative ICG-VA*, performed after temporary occlusion of the aneurysm parent artery or any aneurysmal branch (that may need to be temporary or permanently occluded for final aneurysmal treatment).

Table 1. Primary and secondary identification of cortical recipient artery in selective targeted revascularization by the use of ICG-VA technology.

M4 branches presenting (primarily or secondarily) delayed fluorescence represent suitable bypass recipient arteries. Amongst these cortical M4 branches, the most suitable recipient is chosen on the basis of microsurgical criteria (e.g.: length, width, absence of side-branches).

After the bypass is performed and the aneurysmal lesion is treated (either by clip reconstruction or by partial/complete trapping), a *final ICG-VA* is expected to show symmetric/simultaneous fluorescence of the peri-Sylvian fissure cortical arterial (M4) branches. A flow chart illustrating the technique is presented in Figure 1.

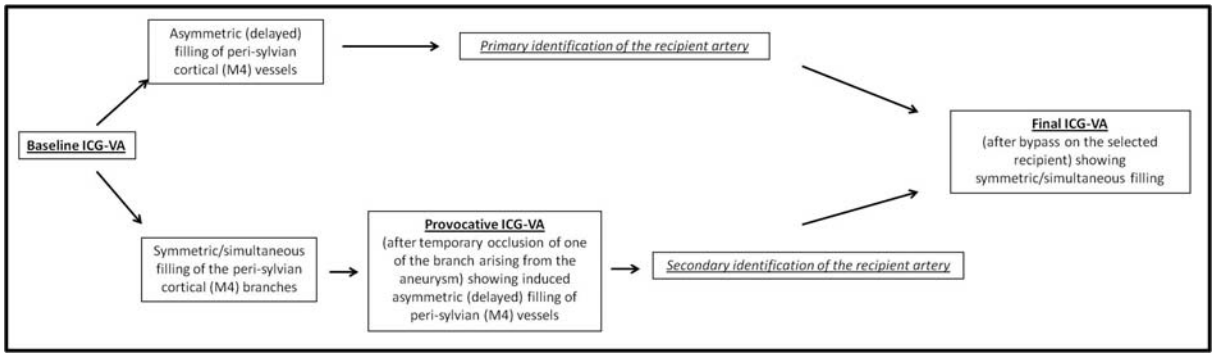

Figure 1. Flow chart illustrating the steps for intraoperative identification of the correct recipient by using ICG-VA technology.

Furthermore, the technique could be applied to identify "uninvolved" cortical arteries, namely peri-Sylvian fissure cortical arteries not representing distal branched of the artery that needs to be occluded for the final aneurysmal treatment. Despite this step is not mandatory because the above described technique is reliable in identifying the correct recipient, it could be useful for further verification, for instance in the case of a complex aneurysm of MCA bifurcation, where the cortical branches of an anterior temporal artery (that arises before the first MCA bifurcation) have to be excluded as possible recipients. This strategy is illustrated in the flow-chart in Figure 2.

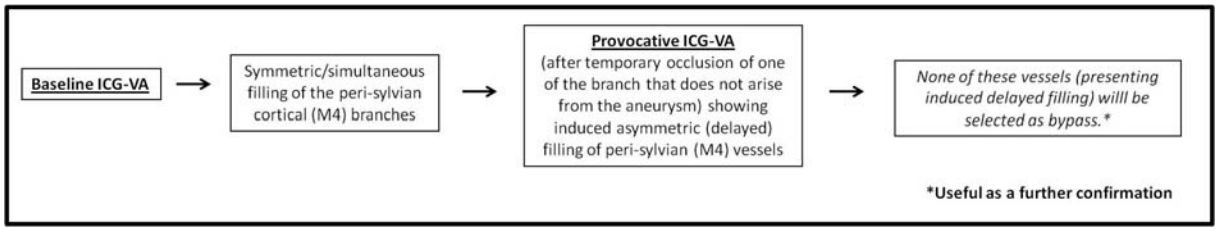

Figure 2. Flow chart illustrating the steps for intraoperative exclusion of erroneous cortical recipients by using ICG-VA technology.

A further proof of the correct revascularization may be obtained by the use of intraoperative flowmetry, because the flow in MCA branch/branches that undergo (temporary or permanently) occlusion for final aneurysm treatment has to match the flow provided by the bypass.

RESULTS

Two illustrative cases are presented. These patients underwent successful treatment of the aneurysm by the use of selective targeted revascularization via ICG-VA technology. The application of the proposed technique allowed reliable identification of the correct recipient artery (cortical branches of the involved MCA segment) and permitted to bypass the correct territory in both patients. After bypass and final aneurysm treatment, the peri-Sylvian fissure vascular territory fluoresced concomitantly (symmetrically and simultaneously) on the final ICG-VA. No complications occurred either because of multiple serial intravenous ICG administrations or because of the temporary occlusion time needed for the provocative ICG-VA (that was always shorter than 2 minutes). There were no ischemic complications and patients had no neurological deficits both after surgery and after 3 months follow up.

Illustrative case 1

A 48-years old man was admitted for the treatment of a calcified partially thrombosed sub-giant MCA aneurysm (M1 bifurcation) and of a small anterior choroidal artery aneurysm (Figure 3 A-D). At the admission, neurological examination was normal. During surgery, the right parietal and frontal branch of the superficial temporal artery (STA) were dissected, a right pterional craniotomy was then performed. After dura opening, the aneurysm was visible at the surface of the Sylvian fissure that was so progressively opened by means of microsurgical techniques. The large thrombosed sack did not allow a safe dissection of the MCA bifurcation and the proximal part of the M2 branches. We therefore decided to perform a superficial temporal artery to middle cerebral artery (STA-MCA) bypass using as a recipient a cortical (M4) branch of the larger inferior M2 segment. To avoid erroneous revascularization, the ICG-VA assisted technique for selective revascularization was applied as follows. After a baseline ICG-VA was obtained to study the cortical peri-Sylvian fissure angioanatomy, a temporary clip was placed on the larger inferior M2 segment and a new provocative ICG-VA was performed. A cortical area showing a delayed fluorescence was clearly evident (Figure 3 E): arteries lying in this zone fluoresced (through retrograde revascularization) during the normal venous phase of the rest of the analyzed peri-Sylvian cortical vasculature (Figure 3 F). The best suitable cortical artery within this area (see arrows in figures 3 F and 3 G) was chosen as recipient and a “protective” STA-MCA bypass was then performed. Therefore we considered safe the exploration of the aneurysm, because the protective bypass supplied the flow in case of prolonged temporary occlusion. With temporary M1 occlusion, we proceeded with intra-aneurysmal thrombus removal until a sharp backflow bleeding was appreciated through the opened aneurysm. Temporary

clips were alternatively placed (temporary) on either M2 trunk, in order to safely complete the thrombectomy/endarteriectomy and to effectively reconstruct the aneurismal base by clips preserving the permeability of the MCA bifurcation and both M2 segments. All the temporary occlusions have been performed on induced hypertension and obviously under the protection of the STA-MCA bypass. Finally the anterior choroidal artery aneurysm was clipped as well. Final ICG-VA showed patency of the bypass and symmetric fluorescence of the peri-Sylvian fissure cortical arteries. At awakening, no neurological deficits were reported. Post-operative neuroimaging (CT-A) performed 72 hours after surgery showed patency of the bypass (Figure 3 H) despite it had competitive anterograde flow and exclusion of the two aneurysms (Figure 3 I). At 3-months clinical follow-up, the neurological examination was normal. No further radiological follow-up was made as the bypass was a protective bypass and the aneurysm exclusion was already confirmed 3 days post-operatively.

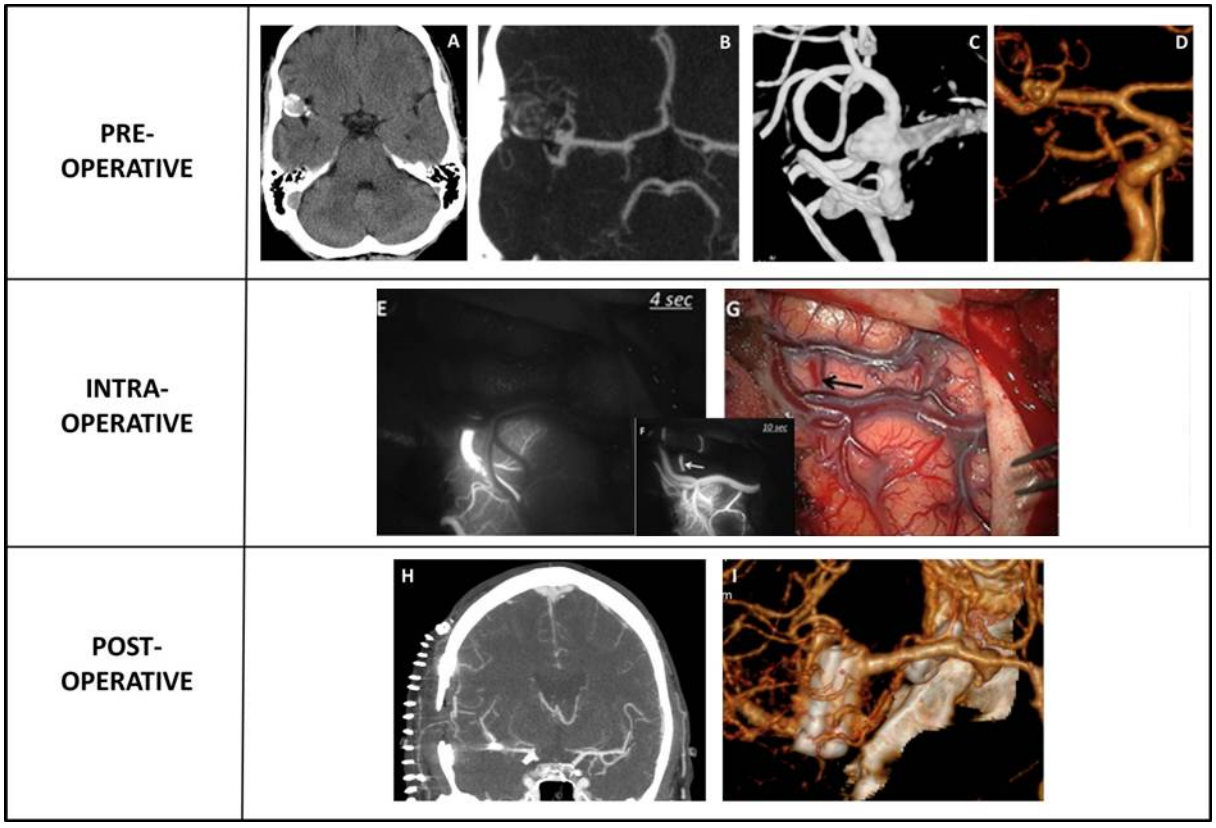

Figure 3

Pre-operative CT (A), CT-A (B) and 3-dimensional DSA (C) documenting a calcified partially thrombosed sub-giant aneurysm of M1 bifurcation and a small anterior choroidal artery aneurysm (D).

Provocative ICG-VA (after temporary occlusion of the inferior M2 trunk) showing asymmetric fluorescence (delayed cortical filling) of a peri-Sylvian fissure area (E). Within this area (whose arteries took fluorescence

during the venous phase of the videoangiography – see fig 1 F), the best suitable cortical artery is targeted as recipient based on microsurgical criteria (see arrows in figure 1 F and 1G).

Post-operative CT-A documenting bypass patency (H) and exclusion of the two aneurysms (I).

Illustrative case 2

A 32-years old man was diagnosed with a fusiform right MCA aneurysm of the M2 bifurcation (Figure 4 A-C). The origin of the aneurysm was bacterial, from endocarditis. At surgery, the parietal STA branch was dissected and a pterional craniotomy performed. After dura opening, dissection of the Sylvian was found extremely difficult and risky due to post-inflammatory dense arachnoidal adhesions between the intra-Sylvian vessels. We therefore decided to avoid total opening of the fissure because of the high risk of vascular injury and to treat the aneurysmal lesion by partial trapping (inflow proximal occlusion) in association with STA-MCA bypass (to revascularize the territory fed by the aneurysmal artery). Flow measurement of the aneurysmal parent vessels was 32 ml/min. To identify a suitable cortical recipient (M4 segment), the ICG-VA assisted technique for selective targeted revascularization was used. In details, after baseline an ICG-VA was registered, a provocative ICG-VA was performed after positioning of a temporary clip on the aneurysm parent artery: asymmetric fluorescence around the Sylvian fissure was evident, with a peri-Sylvian fissure area clearly presenting with a delayed filling. The best suitable arterial recipient lying in this area was chosen as recipient. After removal of the temporary clip on the aneurysm parent artery, the bypass was performed (flow measurement = 11 ml/min). A definitive final clip was then placed on the M2 branch just proximal to the aneurysm, thereafter the bypass flow increased to 29 ml/min. Final ICG-VA showed patency of the bypass and symmetric fluorescence of the peri-Sylvian fissure cortical arteries. At awakening, the patient had no new neurological deficits. Post-operative CT-A 72 h after surgery documented aneurysm disappearance (see figures 4 D and 4 E) and patency of the STA-MCA bypass (Figure 4 F). At 3 months follow-up, a new CT-A confirmed the previous radiological results and neurological examination was normal.

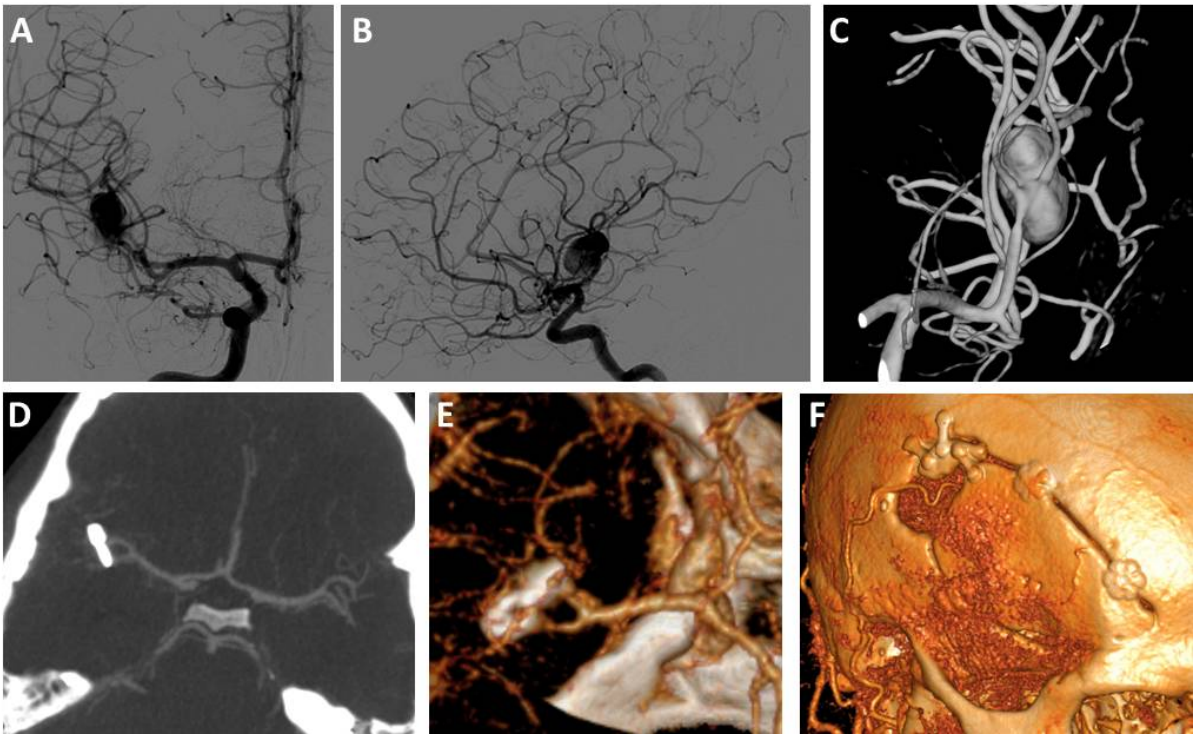

Figure 4

Pre-operative DSA (A, B) with 3-D reconstruction (C) showing a right fusiform MCA aneurysms (M2 bifurcation).

Post-operative CT-A documenting aneurysm disappearance (D, E) and patency of the right STA-MCA bypass (F).

DISCUSSION

Both protective and flow-replacement EC-IC bypass surgery represent a very important tool for the treatment of complex MCA aneurysm [7, 9-10, 13-14]. The aim of the bypass is obviously the preservation of brain perfusion. When a cortical artery is preferred as recipient, its identification is a crucial surgical step. The bypass has in fact to match the distal territory of the involved vessel, namely the recipient has indeed to represent a branch of the occluded MCA branch. In this way either prolonged temporary or permanent occlusion can be executed with minimal ischemic risk. Both combined endovascular/microsurgical (1, 6) or purely microsurgical (5-12) techniques to correct identify the recipient artery in bypass surgery have been recently reported.

In a previous work we already introduced this ICG-VA based technique for selective revascularization. We presented a case series of 7 patients treated for complex MCA aneurysms with selective-targeted EC-IC bypass and illustrated in details three cases. The technique was shown to allow correct identification of cortical recipient

vessels in selective-targeted EC-IC bypass surgery and to eliminate the risk of revascularization of erroneous cortical territories [5]. In the present communication we further describe the possible applications of this technique for selective revascularization and illustrate the surgical decision-making of two different patients treated for complex MCA aneurysms.

As shown, the technique is essentially based on the analysis of fluorescence of peri-Sylvian fissure M4 vessels before (*baseline ICG-VA*) and during temporary clipping (*provocative ICG-VA*) of any MCA branch whose occlusion is needed for final aneurysm treatment. The *provocative ICG-VA* is able to show asymmetric fluorescence among peri-Sylvian fissure vascular arterial territories, namely a territory presenting a delayed cortical filling. M4 vessels lying in the territory and presenting delayed fluorescence activity represent suitable recipients and the best recipient artery can be selected based on conventional microsurgical criteria such as location, size, length, presence of perforators, etc.

In the two reported patients, the information provided by ICG-VA technology allowed the correct identification of the cortical recipient. Both the patients underwent successful treatment of the aneurysm. No ischemic complications were reported and a favorable clinical outcome was achieved in both cases.

This technique enables reliable and accurate identification of the cortical recipient artery and eliminates the risk of revascularization of erroneous territories. It is efficient and can be applied in the management of either proximal or distal complex MCA aneurysms. This technique can also be considered as a step towards reduced invasiveness. In fact a superficial (cortical) bypass is easier, less invasive and safer than a proximal deep one. Easier because working in a deep and narrow operative corridor is definitely more challenging then working on the cortex. Less invasive because it enables reliable targeting of a cortical recipient without the need for dissection of MCA branches along the Sylvian fissure to the cortex. Safer because the tolerance to ischemia is better during the temporary occlusion of a cortical M4 branch as compared with the occlusion of a more proximal M2 or M3 segment. Limitations of this technique essentially consist of the increased operative time (10-20 minutes more), because of the time interval needed between serial ICG-VA runs and the slight temporary occlusion time for the provocative ICG-VA. However, considering this temporary occlusion time was always shorter than 2 minutes, this can be largely accepted in the treatment of complex MCA aneurysms [7, 9-10].

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Disclosure

The authors declare that they have no conflict of interest.

The authors report no personal financial or institutional interest in any of the drugs, materials, or devices mentioned in this article.